Review and Recommendations for TCE Short-Term Action Levels in Indoor Air

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Confusion and misinterpretation is the state of the 2014 regulatory environment as it pertains to short-term trichloroethylene (TCE) action levels for indoor air. The issue starts with comprehension of the United States Environmental Protection Agency's (EPA's) TCE toxicity profile, released in September 2011 (EPA, 2011), that lowered the non-cancer inhalation toxicity value (reference concentration [RfC]) from 10 micrograms per cubic meter (ug/m^3) to 2 ug/m^3. This decrease is equivalent to a 5-fold increase in noncancer risk.

The basis of the 2 ug/m^3 is a controversial study (Johnson et al., 2003), where fetal heart malformations were observed during the 21-day gestational period of the Sprague-Dawley rat based on drinking water (oral) exposure. The concern of this study is that the critical effect occurred from *in utero* exposure (Johnson et al, 2003), which could translate to human cardiac development.

There are several weaknesses with the Johnson 2003 study. EPA's Office of Pollution Prevention and Toxics (OPPT) does not recommend extrapolation from oral to inhalation exposure. Additionally, the fetal heart malformation results could not be replicated in other studies, including one study where TCE was administered via inhalation (Carney et al., 2006), and another study that Johnson collaborated on where TCE was administered via oral dosing (Fisher et al., 2001).

The inability of either study to replicate fetal heart malformation effects, specifically the Carney et al, 2006 inhalation study, introduces significant uncertainty with the Johnson et al., 2003 findings. Study results varied widely, and were not uniformly distributed in the Johnson et al., 2003 study, which infers low confidence in the study itself (Alliance for Risk Assessment, 2013). The questionable toxicity study lends to low confidence in determination of short-term action levels for use in industrial settings. This paper provides a review of a wider literature base on the topic and suggests alternate short-term action levels protective of human health, until such time that EPA Headquarters finalizes their assessment on this topic.

1.0 LITERATURE REVIEW OF TCE TOXICITY

1.1 EPA Toxicity Profile (September 2011)

As mentioned above, EPA's toxicity profile was released in September 2011, with the Johnson et al., 2003 toxicity study as the cornerstone of the new inhalation RfC. The derivation of the inhalation RfC is based on an oral-to-inhalation extrapolated, 99th percentile Human Equivalent Concentration (HEC_{99}) to the rat internal Benchmark Dose-low (BMDL) associated with a 1% extra risk to each rat pup (BMDL01) (IRIS, 2014). This $HEC_{99,BMDL01}$ concentration of 21 ug/m^3 protective of lifetime continuous exposure, is then divided by an uncertainty factor of 10, to arrive at EPA's inhalation RfC (2 ug/m^3) (Integrated Risk Information System [IRIS], 2014).

The toxicity profile for TCE is presented on EPA's IRIS website (IRIS, 2014) and states that "the RfC is an estimate (with uncertainty spanning perhaps an order of magnitude) of a *continuous inhalation exposure* to the human population (including sensitive subgroups) that is likely to be without an appreciable *risk of deleterious effects during a lifetime*". Therefore, intent of the inhalation RfC is to protect against lifetime risk from continuous inhalation exposure, which is not representative of short-term exposure or conditions requiring immediate action/removal.

1.2 ATSDR Studies

The mission statement of the United States Department of Health and Human Services, Agency for Toxic Substances and Disease Registry (ATSDR) is to "serve the public through responsive public health actions to promote healthy and safe environments and prevent harmful exposures" (ATSDR, 2009). As noted on their website, http://www.atsdr.cdc.gov/about/mission_vision_goals.html, ATSDR's goals include:

- Protecting the public from environmental hazards and toxic exposures;
- Advancing the science of environmental public health, through:
    - Collection, analysis, and data summarization on environmental exposures and health; and
    - Conducting research to identify associations between environmental exposures and health risks.
- Educating communities, partners and policy makers about environmental health risk and protective measures; and
- Providing unique scientific and technical expertise to advance public health science and practice, through:
    - Collaborative laboratory research that yields:
        - Critical population-level data;
        - A greater understanding of adverse health outcomes; and
        - Information to evaluate public health interventions.

Based on the mission and goals of the ATSDR, evaluating short-term exposure and health effects of TCE is within their authority. In 2013, ATSDR released a Health Consultation study regarding the Millsboro TCE Site, located in Millsboro, Delaware. At this site, drinking water was contaminated with TCE from October 2004 for approximately one year, at which point, a water treatment filter was installed to remove the TCE from the drinking water. The purpose of the ATSDR Health Consultation was to determine whether or not TCE exposure during that timeframe was a human health concern (ATSDR, 2013a).

In order to evaluate the inhalation exposure pathway, ATSDR assumed that residents would be exposed to TCE in groundwater that volatized during showering or other household uses such as dishwashing or laundry, during a time period of no more than one year. ATSDR's Health Consultation indicated that "*there is no suitable comparison values for TCE that represent the (one-year) timeframe in which the Millsboro residents were exposed…EPA's reference dose and reference concentration are both intended for comparison to chronic or longer duration exposure scenarios. ATSDR used the Human Equivalent Concentration (HEC_{99}) for inhalation during showering. The HEC is the concentration derived from animal studies that takes into account the physiologic and pharmacokinetic differences in animal models and man.*" Note that this HEC_{99} of 21 ug/m^3 is the same value that was derived from the Johnson et al., 2003 study (despite the uncertainty surrounding the study) and was used to compare against calculated 24-hour average indoor air concentrations of TCE to determine whether health effects were a concern (ATSDR, 2013a). This study evaluated residential exposure and determined a maximum allowable 24-hour (continuous) indoor air concentration of 21 ug/m^3 for TCE. Therefore, using the same concentration of TCE (21 ug/m^3) is protective of lesser-exposed receptors, such as an indoor worker, for an intermediate

period of time (e.g., a year).

In 2013, ATSDR also released a Public Health Assessment regarding the Pohatcong Valley Groundwater Contamination Superfund Site, located in Warren County, New Jersey. At this site, the public was exposed to drinking water contaminated with TCE from 1972 to 1981, when treatment systems were put into place (ATSDR, 2013b). Similar to the Millsboro Site, the Pohatcong Site assumed that residents would be exposed to TCE in groundwater that volatilized during showering. Therefore, ATSDR calculated time-weighted average (TWA) indoor air concentrations based on showering activities and compared them to the 21 ug/m^3 HEC_{99} (the Lowest Observed Adverse Effect Level, or LOAEL) of the Johnson et al, 2003 study (ATSDR, 2013b), despite the uncertainty surrounding this study. Similar to the Millsboro study, this risk assessment indicates that 21 ug/m^3 is a reasonable, allowable TWA indoor air concentration for residents over a period of approximately 10 years. Therefore, a TCE concentration of 21 ug/m^3 would also be protective of lesser-exposed receptors, such as an indoor worker.

1.3 Toxic Substances Control Act Recommendations

In December 2012, EPA's Office of Chemical Safety and Pollution Prevention (OCSPP) released a "Draft do not cite or quote, Toxic Substances Control Act (TSCA) Workplan Chemical Risk Assessment for Trichloroethylene: Degreaser and Arts/Crafts Uses" (EPA, 2012a). In reviewing inhalation toxicity studies for TCE in this document, EPA's OPPT chose to disregard the Johnson et al., 2003 study because it was not inhalation-based. Instead, they identified 12 inhalation-based toxicity studies, which resulted in much higher levels than 21 ug/m^3 for critical effects. Specifically, the HEC_{99} values from the 12 inhalation studies ranged from 0.013 parts per million by volume (ppmv) (69.8 ug/m^3) to 120 ppmv (644,460 ug/m^3) (EPA, 2012a).

2.0 REGULATORY REVIEW

Given the uncertainty surrounding the Johnson et al., 2003 study and EPA's route extrapolation to arrive at an inhalation RfC of 2 ug/m^3 for chronic exposure, this paper explores alternate short-term action levels protective of intermediate exposure periods similar to the ATSDR Millsboro study, as well as conditions requiring immediate action/removal. The remainder of this section presents a regulatory review of how risk-based indoor air levels for TCE have been determined.

2.1 Risk-Based Remediation Goal (RBRG) vs. Removal Action Level (RAL)

The terms "Risk-Based Remediation Goal" (RBRG) and "Removal Action Level" (RAL) are used frequently among regulatory agencies when identifying concentrations protective of indoor air exposure. The RBRG is protective of long-term, chronic indoor air exposure, while a RAL is focused on short-term conditions requiring immediate action. The noncancer Hazard Quotient (HQ), which is a ratio of the exposure level to a screening value, is lower when calculating an RBRG (which assumes an HQ of 1.0 per EPA's *Risk Assessment Guidance for Superfund, Volume I. Human Health Evaluation Manual, Part B: Development of Risk-Based Preliminary Remediation Goals* (EPA, 1991)) versus calculating an RAL (which assumes an HQ of 3.0, per EPA's *Revised Superfund Removal Action Levels memorandum* (EPA, 2008). The intention of the 3-fold increase in HQ for RAL development is to allow a cushion between long-term health protectiveness and short-term immediate action. Therefore, for purposes of setting a short-term immediate action level for TCE, an HQ of 3.0 is appropriate as recommended by EPA (EPA, 2008). Screening levels based on ATSDR's Millsboro and Pohatcong Valley findings, as well as published EPA values, are summarized in Table 1.

TABLE 1: Summary of Risk-Based TCE Indoor Air Levels

Source	Screening Levels and RALs	Basis for Concentration*
Intermediate Residential Exposure (ATSDR, 2013a; 2013b)	TCE = 21 ug/m^3	Based on HEC_{99}, assumed protective of intermediate (1 year) residential exposure
EPA Indoor Worker Regional Screening Level (RSL) (EPA, 2013a)	TCE = 8.8 ug/m^3	Based on long-term worker exposure) 8-hour workday, 250 days per year for 25 years), inhalation RfC (2ug/m^3), HQ = 1.0
EPA Region 9 RAL (EPA, 2012b)	TCE = 15 ug/m^3	Based on acute (short-term) 10-hr workday, inhalation RfC (2ug/m^3), HQ = 3.0
EPA Region 10 Short-Term Concentration (EPA, 2012c)	TCE = 8.4 ug/m^3	Based on 21-day exposure period, inhalation RfC (2ug/m^3), HQ = 1.0**
EPA Region 9 Prompt Response Action Level (EPA, 2013b)	TCE = 9 ug/m^3 (8-hour workday); TCE = 7 ug/m^3 (10-hour workday)	Based on short-term exposure, inhalation RfC (2ug/m^3), HQ = 1.0**

* Both the HEC_{99} and RfC used to determine screening levels and RALs were calculated using the Johnson et al., 2003 study. However, as described above, these inhalation-based values are extrapolated from an oral exposure study, which EPA's OPPT does not recommend. Furthermore, the Johnson study results varied widely, indicating a high degree of uncertainty. Finally, no other study has been able to replicate the toxicological, critical effects observed in the Johnson study.

** HQ of 1.0 is not consistent with EPA (2008) HQ of 3.0

3.0 RECOMMENDATIONS FOR SHORT-TERM ACTION LEVELS IN INDOOR AIR

Based on a review of available indoor air levels protective of an indoor worker, it is apparent that the Johnson et al., 2003 study and the HEC_{99} value of 21 ug/m^3 are used as either the ultimate goal (in the case of the two ATSDR studies) or the basis of the inhalation RfC (2 ug/m^3), despite the uncertainty surrounding the Johnson study. The variability in the indoor air levels presented in Table 1 is due to different HQ values. Using an HQ of 3.0 is consistent with approved methodologies per EPA (2008) guidance when setting RALs; however, the EPA Region 9 Prompt Response Action Level and the EPA Region 10 Short-Term Concentration are both based on an HQ of 1.0, which is not consistent with the standard approach for setting a RAL. The use of an HQ = 1.0 is considered appropriate when evaluating long-term, chronic exposure; thus, the EPA Indoor Worker RSL is correctly derived using an HQ = 1.0.

Based on this review, two short-term TCE action levels protective of an indoor worker are recommended:

- ATSDR's use of the HEC_{99} (21 ug/m^3) for intermediate residential exposure, which would also be protective of short-term worker exposure for intermediate periods (e.g., one year) (ATSDR, 2013a; 2013b);

- Adjusting the HQ from 1.0 to 3.0 for EPA's indoor worker RSL of 8.8 ug/m^3 to calculate an indoor worker RAL of 26.4 ug/m^3 (8.8 ug/m^3 x 3.0) representative of short-term conditions requiring immediate action.

The ATSDR concentration of 21 ug/m^3 would certainly also protect intermediate residential exposure, as the resident was the receptor both ATSDR studies were designed to protect. Both of these recommended values (21 and 26.4 ug/m^3) are similar, which lends confidence in using this concentration range for short-term indoor air action levels for TCE, instead of relying on risk-based concentrations protective of chronic, long-term inhalation exposure, which are not representative of intermediate periods up to one year or for conditions requiring immediate action/removal. Regardless of which concentration is chosen, the lack of inhalation studies producing fetal heart malformations should be revisited by EPA prior to setting a policy decision on indoor air action levels for TCE.

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